Guidance For the Technical Content of a Premarket Approval (PMA) Application for an Endolymphatic Shunt Tube With Valve

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Preface

This guidance is intended to aid applicants in the preparation of PMAs for endolymphatic shunt tubes with valve. The guidance describes the kind of preclinical and clinical information needed to allow the agency to evaluate the safety and effectiveness of these devices. The format and specific contents are described in detail in the Premarket Approval (PMA) Manual, FDA 87-4214.

Wherever possible, an application should follow the guidance presented here and provide an explanation of any omission to avoid unnecessary questions from the Center. The submission of PMAs which contain all necessary information will expedite the review and approval of these applications.

This guidance is subject to future updates and revisions, as they become necessary. If there are any question of comments concerning this guidance, please contact Lillian Yin, Ph.D., Director, Division of OB GYN, ENT and Dental Devices, Office of Device Evaluation, Center for Devices and Radiological Health (HFZ-470), Food and Drug Administration, 8757 Georgia Avenue, Silver Spring, Maryland 20910, telephone (301) 427-7555.

I. Preclinical Investigations

A. Preclinical investigations should state that the study was conducted in compliance with Good Laboratory Studies, CFR Part 58. If not, give a brief statement of the reason for the noncompliance.

B. Investigations can be in vitro, in vivo or histopathogical and can pretain to diagnostic methods, etiology, function of the endolymphatic sac, correlation of endolymphatic hydrops with vertigo or deafness, etc.

1. Animal studies could include:

a. Development of animal models for vertigo and endolymphatic hydrops [Shark, fish, guinea pig, rabbit, and cat models have been reported in the literature.];

b. Histopathologic studies correlating experimentally induced endolymphatic hydrops with inner ear pathology;

c. Studies correlating auditory sensitivity and acoustic distortion with experimentally induced endolymphatic hydrops;

d. Studies to determine actual pressure of endolymph and perilymph within the inner ear, especially within the endolymphatic sac, as well as possible mechanisms of pressure regulation;

e. Investigations into the function and fluid mechanics of the endolymphatic sac and duct;

f. Investigations into the correlation of electrophysiological measurments with endolymphatic hydrops; and

g. Determination of biocompatibility of materials to be implanted.

2. Pre-clinical human studies should include:

a. Histologic studies employing both light and electron microscopy of the temporal bones from patients documented with vertigo or Meniere's disease to determine histopathology and to correlate morphology with development of vertigo and hearing impairment [Light and electron

microscopy studies of normal temporal bones should be included.];

b. Investigations of function of endolymphatic sac and duct;

c. Determination of normal or usual course of Meniere's disease; and

d. Determination of possible mechanisms of pressure regulation and fluid mechanics within the human endolymphatic sac.

C. Can be a survey of pertinent literature.

II. Clinical Investigations

A. Patient selection is critical to the successful clinical investigation of the risks and benefits of the implantation of the endolymphatic shunt tube with valve. The significant factors are the presence of the classic symptoms of vertigo, hearing impairment and tinnitus, test results, the possibility of bilateral disease, and the choice of controls.

1. The patients should exhibit the following symptoms:

a. Episodic vertigo with nausea and vomiting;

b. Fluctuating and progressive sensorineural hearing loss, often low-frequency;

c. Tinnitus;

d. Sensation of aural fullness (not always present); and

e. History of allergies (not always present).

2. Symptoms must be refractory to medical (non-surgical) treatment.

3. Uniformity in patient selection and post implantation assessment would be facilitated by the following tests.

a. Serial audiograms at 500 HZ, 1 kHZ, 2 kHZ, and 3 kHZ to determine the worst preoperative hearing 6 months before sac surgery;

b. Cochlear profiles for both ears based on the worst Pure Tone Average (PTA) at 250 cps, 500 cps, and 1000 cps;

c. The Glycerol Test in both ears (a positive is considered indicative of successful implantation);

d. Vertigo disability profile based upon patient history, caloric or rotary chair testing; and

e. Patient history of tinnitus and aural fullness.

4. The possibility or presence of bilateral Meniere's Disease must be determined. The prevalance of bilateral disease increases with the duration of disease and appears to correlate with age of onset, especially early onset.

5. The presence of any anatomical abnormalities which preclude implantation of the endolymphatic shunt tube with valve should be determined.

6. Controls should be statistically valid in number.

a. Good preoperative assessment is essential so that patient as own control.

b. Controlled clinical studies must be designed to comply with the Helsinki Agreement on Medical Ethics.

B. Surgical protocol

1. Surgery should be preceded by tomographic examination of the endolymphatic duct and sac.

a. Permits visualization of surgical area.

b. Eliminates patients with small chance of successful implantation due to too small a duct, lack of the sac or duct, or an antomical abnormality of the cochlea or vestibular structures.

2. Surgical technique for implantation of the endolymphatic shunt tube with valve has been well described by Arenberg in 1979 with later modifications published in 1982.

3. Transtympanic electrocochleography monitoring during implantation sugery to ascertain that endolymphatic duct and sac have been successfully opened. (Optional)

C. Evaluation of safety and effectiveness of implant.

1. Clinical study should included 100% follow-up of all

patients for one year after implantation of the shunt tube.

2. Current investigators should report results in compliance with the AAO-HNS: Committee on Hearing and Equilibrium Guidelines for Reporting Results in Meniere's Disease, 1985.

3. Previously published work should report results in compliance with, the AAO-HNS: Meniere's Disease: Criteria for diagnosis and evaluation of therapy for reporting results: 1972.

4. Both pre- and postoperative best hearing level should be assessed using PTA as well as hearing at low and high frequencies.

5. All complications must be reported, including those listed below:

a. Iatrogenic ears;

b. Any infections including middle ear infections;

c. Cerebro-spinal fluid leaks;

d. Clogged tubes; and

e. Migrated or misplaced tubes.